23. (amended) A method of purifying the autotaxin polypeptide of claim 20 or 21, comprising the steps of:

i) collecting and concentrating supernatant from cultured [A2058 human melanoma] cells whereby a first preparation of said polypeptide is produced;

ii) salt fractionating said first preparation to produce a second polypeptide preparation;

iii) isolating said polypeptide from said second preparation so that said polypeptide is obtained in substantially pure form.

25. (amended) The [A recombinant] autotaxin polypeptide according to claim 20 or 21, wherein the polypeptide is produced recombinantly.

26. (new) The isolated polypeptide according to claim 20, wherein the polypeptide comprises the amino acid sequence Tyr-Met-Arg-Pro-Val-Tyr-Pro-Thr-Lys-Thr-Phe-Pro-Asn.

27. (new) The isolated peptide according to claim 26, wherein the polypeptide is from about 788 amino acids to about 979 amino acids in size.

REMARKS

Support for the amendment to claim 20 finds support throughout the specification; for example, at page 20, second paragraph through page 21, third paragraph and at page 5, second full paragraph. Support for the amendment to claim 21 is supported by the specification, for example, at page 10, last paragraph. Support for the amendment to claim 23 finds support throughout the specification, for example, at page 13, second full paragraph. Support for the amendment to claim 25 is supported by the specification, for example, at page 4, third paragraph and page 13, second full

paragraph. Support for new claim 26 is found throughout the specification, for example at page 10 under the description of Figure 18 and in Figure 18 which describe and show the putative phosphodiesterase active site. Support for new claim 27 is found throughout the specification, for example, in the sequence listing which shows an autotaxin with 788 amino acids (SEQ ID NO: 36) and an autotaxin with 979 amino acids (SEQ ID NO: 38).

RESPONSE TO SECTION 112 REJECTION

Claims 20-25 were rejected under 35 U.S.C. §112, second paragraph, for being indefinite for failing to distinctly claim subject matter. Applicants respectfully disagree with this ground of rejection.

In particular, the Examiner contends that in claim 20 the recitation "wherein said polypeptide thereof has cell motility activity" is unclear as to whether the polypeptide has motility or whether the polypeptide has the ability to regulate the motility of something else. If the peptide regulates something else, the Examiner queries "what is the something that is being moved absent a structure which is defined by the amino acid sequence?" Applicants have amended claim 20 by deleting the phrase "wherein said polypeptide thereof has cell motility activity" and replacing it with the phrase "wherein said polypeptide is a cell motility-stimulating polypeptide." Applicants have also added the description that the amino acid sequence of human autotoxin has "phosphodiesterase activity." Thus, it is clear that the polypeptide regulates cell motility not peptide motility.

Claim 21, is considered indefinite because "where claim 20 does not define the structure it is not apparent whether or not cell motility activity is retained by the claimed but undefined fragment." Applicants have deleted the phrase "wherein said polypeptide is a fragment thereof having at least 5 amino acids" and have replaced it with the phrase "wherein said polypeptide comprises a phosphodiesterase active site."

Claim 22 is considered indefinite because "it is not apparent how cell motility is retained when the protein is bound to a solid support." Applicants attach as Exhibit 1, Chapter 9.6 of the *Biochemical Engineering and Biotechnology Handbook*, Second Edition, 1991, Stockton Press, which describes how polypeptides can be immobilized and still maintain their activity.

Claim 23 is considered indefinite for reciting "substantially pure" with respect to the polypeptide. Applicants assert that in view of the status of the art, the phrase "substantially pure" reasonably apprises one skilled in the art of the scope of the invention. For example, claim 1 of U.S. Patent No. 4,935,497 describes an agent "comprising a substantially pure polypeptide." Claim 1 of U.S. Patent No. 4,956455 describes a "substantially pure basic fibroblast growth factor." Thus, it is evident that what constitutes "substantially pure" it is readily apparent to one skilled in the art.

Claim 25 is considered indefinite for reciting "a recombinant autotoxin." Applicants have amended claim 25 to describe a polypeptide that "is produced recombinantly." The production of recombinant polypeptide is described in, for example, Mantiatis et al. *Molecular Cloning A Laboratory Manual*, 1982, Cold Spring Harbor Laboratory.

In light of the amendments and arguments presented above, applicants request reconsideration and withdrawal of the Section 112 rejection.

RESPONSE TO SECTION 102 REJECTION

Claims 20-25 were rejected under 35 U.S.C. §102(b) for being anticipated by Stracke et al. U.S. Patent No. 5,449,753. Applicants respectfully disagree with this ground of rejection.

The present application, Serial No. 09/483,831 was filed January 17, 2000. The present application is a Continuation of Serial No. 08/977,221, filed November 24, 1997, which is a Division of application No. 08/346,455, filed November 28, 1994, which is a Continuation-In-Part of application No. 08/249,182, filed May 25, 1994, which is a Continuation-In-Part of application No.

07/822,043, Filed January 17, 1992 which issued as U.S. Patent No. 5,449,753.

The subject matter of the present specification claims priority, at least, to application No. 08/346,455, filed November 28, 1994. Thus, U.S. Patent No. 5,449,753 cannot anticipate applicants' claims since U.S. Patent No. 5,449,753 published September 12, 1995. Therefore, applicants request reconsideration and withdrawal of the Section 102 rejection.

AUTHORIZATION

No additional fee is believed to be necessary. However, the Commissioner is hereby authorized to charge any additional fees which may be required for this amendment, or credit any overpayment to Deposit Account No. 13-4500, Order No. 2026-4149US4.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 2026-4149US4. A DUPLICATE OF THIS SHEET IS ATTACHED.

Respectfully submitted,

MORGAN & FINNEGAN, L.L.P.

Dated: November 15, 2000

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